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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/822,949	CHANG, RONG-KUN	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7,14,15,17 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,7,14,15,17 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *7/10/09* .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt of amendment and remarks filed 11/16/09. Claims 3 and 16 are canceled. Claims 1, 5, 7, 14 and 15 are amended. Claims 1, 4, 5, 7, 14, 15, 17 and 18 are pending.

Status Identifiers: Claim 14 is currently amended but the status identifiers states "previously presented." It is respectfully requested that applicant use the appropriate status identifier for the claims in all future claim listings.

Response to Arguments

1. Previous rejections that are not reiterated herein are withdrawn. For example, applicant's argument on page 5 of the remarks that the homogeneous matrix of claim 1 (i) comprises … accommodates the matrix to be open to other components is persuasive. The previous rejection that the consisting language is exclusionary to granulating agents, say, is not based on the method of manufacture of the composition, but, rather, it was based on applicant's disclosure where al the products have granulating agents.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 4, 5, 7, 14 15, 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejections.

4. Amended claim 1 requires a sustained release pharmaceutical to consist of a homogenous matrix. Applicant has said that Example 1 provides support for "homogeneous." However, the specification even in Example 1 does not say that blending and granulation provides a homogeneous matrix. The original claims and the specification as a whole do not provide support for a homogeneous matrix and as such does not envision a homogenous matrix.

5. Amended claim 1 now says that the active agent "when swallowed, is released gradually over en extending time period." Original claim 1, which provides the only support for swallowing says, "...whereby the active agent is released and swallowed gradually over an extended time period ... tract." This recitation does not appear to be same as "when swallowed, is released gradually over en extending time period," as now recited in amended claim 1. therefore, "when swallowed, is released gradually over en extending time period," was not envisioned at the time the original specification was filed.

6. Amended claim 1 now requires the active agent to be "solely" absorbed in eth upper GI tract. Various sections of the original specification do not envision that the active agent is solely absorbed in the upper GI tract. What was envisioned is that "Doxycycline is rapidly and almost completely absorbed from the upper portion of the gastrointestinal tract following oral administration in conventional dosage forms," in paragraph [03] of the specification as filed. What was also envisioned is that trospium chloride has a bioavailability of approximately 10% (see paragraph [03] as originally filed. The original specification does not envision that the

active agent is entirely absorbed in the upper GI tract, which is what "solely" represents to the exclusion of other areas where the active agent may be absorbed.

7. Correction and/or explanation are respectfully requested.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 4, 5, 7, 14, 15, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Faour et al. (US 6,004,582) for reasons of record with a modification to address the current amendment.

10. Faour discloses a multi-layered delivery device (abstract), that is "useable in different environments for use of the osmotic device include biological environments such as the oral, ocular, nasal, vaginal, glands, gastrointestinal tract, rectum, cervical, intrauterine, arterial, venous, otic, sublingual, dermal, epidermal, subdermal, implant, buccal, bioadhesive, mucosal and other similar environments. Faour contemplates use of the device in different environments by stating, "likewise, it may be used in aquariums, industrial warehouses, laboratory facilities, hospitals, chemical reactions and other facilities" (column 4, lines 34-42). The dosage form is in the form of a tablet, pill, sphere, bar, plate or granule (column 6, line 7). The core of the tablet can comprise a number of agents such as osmagents, buffering agents, antioxidants, acacia, alginic acid, polyvinylpyrrolidone, methylcellulose, polyethylene glycol and many more that can

be used with active agents in tablet formulation (column 9, line 28, 38-65; column 10, lines 14-57) and these materials such as acacia, the alginic acid, the polyvinylpyrrolidone used in the core or matrix of tablets meet the polymer requirements of claim 1 and claim 17. The recitation that the pharmaceutically or nutritionally active agent "is not absorbed through the oral mucosa to a substantial extent" now recited in claim in claim 1 is a property of the composition with a note that substantial is relative. The process of preparation of the dosage form is exemplified in at least Examples 1-4 and method claim 14 reads on Faour's method. Faour formulates a number of active agents as multilayered tablets (column 13, line 38 to column 16, line 44) and included in this list is riboflavin (column 16, line 31) with the teaching of the riboflavin meeting claim 7. The polyvinylpyrrolidone, methylcellulose and polyethylene glycol meet the limitation of claim 17. The retaining means is a mucoadhesive and at least the hydroxypropylmethyl cellulose of Faour (column 6, line 26) meets the mucoadhesive of claims 4 and 15 and thus the retaining means of claims 1, 5 since claim 5 defines the retaining means as a holding device. At least the ethyl cellulose (column 6, line 27) meets claim 18. The sustained release matrix composition of claim 1 reads on the layered dosage of Faour since each layer contains a matrix.

Response to Arguments

11. Applicant's arguments filed 11/16/09 have been fully considered but they are not persuasive.

12. Applicant argues that the Faour teaches semipermeable membrane that is not in the claimed invention. While the examiner agrees with the applicant that the claimed matrix composition does not have a semipermeable membrane, it is noted that the matrix composition is recited to comprise of … and the comprising language is open and does not exclude the presence

of a membrane as disclosed in Faour. Furthermore, the membrane of Faour is made up of polyethylene glycol (column 3, lines 57, 58) that also meets the limitation of muco-adhesive, the retaining means of the claims

13. Claims 1, 4, 5, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Schiraldi et al. (US 4,713,243) for reasons of record and modified to address the amendment.

14. Schiraldi discloses bioadhesive extruded single or multilayered thin film for intra oral controlled releasing delivery (abstract; column 2, lines 22-27) for a number of therapeutically active agents such as doxycycline hyclate (column 3, line 51) with the doxycycline hyclate anticipating the generic pharmaceutically active agent of claim 1. The film composition adheres to the mucous membrane; the film, which is single or multilayered layered comprises water soluble or water swellable polymer matrix bioadhesive layer (column 2, lines 30-35), optionally contains reservoir and/or outer protective barrier membrane (column 2, lines 52-55), therapeutic agent contained in all the layers (column 2, lines 55-63). Polyethylene oxide and hydroxypropyl cellulose are film forming polymers of Schiraldi (column 3, lines 14 and 15). The polyethylene oxide and hydroxypropyl cellulose are listed in claim 17 as the hydrophilic polymers of claim 1. The hydroxypropyl cellulose or homopolymer of ethylene oxide makes up the bioadhesive layer that adheres to the mucous surface (column 2, lines 35-37) so that the requirement for a retaining means of claim 1, which is further defined in claim 4 as a mucoadhesive is met as well as the retaining means of claim 5 because the holding device is the retaining means and mucoadhesive according to claims 4 and 5. The recitation that the pharmaceutically or nutritionally active agent "is not absorbed through the oral mucosa to a substantial extent" now recited in claim in

claim 1 is a property of the composition with a note that substantial is relative. The bioadhesive layer also contains water insoluble polymers such as ethyl cellulose, propyl cellulose, polyethylene and polypropylene (column 2, lines 48-41; column 3, lines 21-25) meeting the inert plastic of claim 1 that is further defined in claim 18 such that the ethyl cellulose and polyethylene of Schiraldi meet claim 1 and new claim 18. Thus Schiraldi anticipates claims 1, 4, 5, 17 and 18.

Response to Arguments

15. Applicant's arguments filed 11/16/09 have been fully considered but they are not persuasive.

16. Applicant argues that the absorption of drug in the instant invention does not happen in the oral cavity but solely in the GI tract and that Schiraldi does not disclose a pharmaceutical preparation for systemic absorption.

17. The examiner disagrees. The recitation that the active agent is not absorbed through the oral mucosa to a substantial extent is relative because "substantial" is a relative term and the specification has not defined what is substantial in order that Schiraldi may be excluded as art. Furthermore, systemic absorption implies absorption into the circulatory system. As far as the examiner may note in Schiraldi, the drugs or active agents disclosed by Schiraldi, such as anesthetics, anti-inflammatories, anti-histamines, antibiotics and others (see column 3, lines 42-56) are all capable of systemic delivery or systemic absorption. The active agent being absorbed solely in the upper GI tract is characteristic of the active agent and since the generic active agent of claim 1 exhibits that property, the active agent of Schiraldi would also exhibit that property.

18. Claims 1, 4, 5, 7, 14, 15, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Lerner et al. (US 6,197,331).

19. Lerner discloses controlled release solid composition for the oral cavity or pharmaceutical oral patch (abstract) with the disc of claims 14 and 15 reading on the patch; the composition contains adhesive and release layer (column 8, lines 20-25) meeting the requirement for layered dosage form in which one surface is adhesive, thus meeting claim 4 and another surface, non-adhesive (column 7, lines 53 and 54); polymer in the adhesive layer is EUDRAGIT type polymer (column 11, lines 24 and 25; column 7, lines 25-28, 45-50); the matrix can also contain plasticizers such as polyethylene glycol, castor oil (column 11, line 66 to column 12, line 5) with the polymer or the oil meeting claim 17. Lerner specifically teaches that "any agent can be used, depending on the purpose of therapy" (column 15, lines 12 and 13) and proceeds to name specific ones and cyclosporin is mentioned as a peptide or protein drug (column 16, lines 52-56) meeting the generic active agent of claim. The mixing of the polymer with the active agent and eventually formulating the composition into patch (column 17, lines 26-34) meets the requirements of the method claims 14 and 15. The recitation that the composition "is not absorbed through the oral mucosa to a substantial extent is a property of the composition so that Lerner meets the claim limitation of claim 1. Lerner thus teaches all the limitations of the designated claims. The adhesive material which includes EUDRAGIT (column 11, lines 16-53) meets claim 4 and thus the retaining device of claims 1, 5 and 15 is met. Other polymers such as polyacrylate, polymethacrylate, cellulose derivatives, ethylcellulose, hydroxypropylmethyl cellulose, cellulose acetate phthalate, polysaccharide, guar gum, pectin, alginic acid and salts thereof, xanthan gum, gum tragacanth, gum arabic, starch, chitin, chitosan, proteins, polyamino

acids, polypeptides, gelatin, polyglycolic acid, polylactic acid, polyglycolic-polylactic copolymers, cross-linked polysaccharides, and cross-linked protein (column 11, lines 16-23) and when ethyl cellulose is used, claims 1 reciting inert plastic as the polymeric material and claim 18 defining what the inert plastic is are met.

Response to Arguments

20. Applicant's arguments filed 11/16/09 have been fully considered but they are not persuasive.

21. Applicant argues that the invention is directed to drugs that are not intended to absorb through the oral mucosa to any appreciable extent and that Lerner requires the drugs to be absorbed through the mucous membrane in the oral cavity according to column 4, 6th paragraph.

22. The examiner agrees that Lerner intended to overcome the prior art, which is what the applicant has identified in column 4, paragraph 6 as "moreover, the known preparations are usually composed of components which are soluble or disintegrable within the mouth. Thus, the pharmaceutically active agents contained in the preparations are mostly swallowed without being absorbed through the mucous membrane in the oral cavity. Thus, these preparations are not completely satisfactory as a sustained- or controlled-release preparation for the oral cavity." However, Lerner resolved the above by using polymers that delayed the release and ensured systemic delivery (Column 7, lines 3 and 4). Further, "appreciable extent" as stated by applicant and in the specification at page 4, paragraph [09] is relative and the specification has not defined what "appreciable extent" means or is. Thus, because appreciable is relative, Lerner's composition is not excluded.

23. Applicant also argues that Lerner's preparation is a liquid that is eventually solidified while by contrast the invention requires distinct polymer particles.

24. While amended claim 1 says particles of polymeric material, it is also noted that claim 1 says fat-wax matrix material or particles of polymeric material. Castor oil and tributyl citrate, a fatty acid ester (see column 12, lines 2 and 3of Lerner) meets the fat-wax. Further also, Lerner anticipates an embodiment in which the polymer and the drug are associated as physical dispersions (column 10, lines 50-53).

25. Therefore, the rejection is maintained.

Other matters

26. While original claim 6 recites that the pharmaceutically or nutritionally active agent is not absorbed through the oral mucosa to a substantial extent, the original specification does not provide antecedence for the claim terminology now in claim 1.

27. Further also, the specification does not say that holding device is equivalent to a retaining means.

28. No claim is allowed.

29. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

30. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

31. **Suggestion**: Original specification at paragraph [30] describes a holding device that is a plastic holder with string that can be used to retain the dosage form in the oral cavity. Applicant may consider amending the claim to use the plastic holder with the string as a device for holding the dosage form in the oral cavity. It is also suggested that applicant amend the claims to remove the new matter from the claims, amend the specification so that the specification provides antecedent support for original claim limitations in original claim 6.

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on Monday to Thursday from 7 a.m. to 5:30 p.m.

33. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

34. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Blessing M. Fubara/
Primary Examiner, Art Unit 1618